OIPE JC200 JUN 2 7 2003 PATENT & TRADEMARK OFFICE

IN THE SPECIFICATION:

Please amend the specification as follows:

At page 26, after paragraph 66, please insert the printed Sequence Listing submitted herewith.

Replace current paragraph 5 at page 2 with the following paragraph:

-- In the various EVH1 binding proteins, the EVH1 domains of the Ena/VASP protein family recognize proline-rich peptide sequences having an FPPPP (SEQ. ID. NO. 1) core motif, which are folded in the form of a polyproline helix of type II. EVH1 binding proteins having such FPPPP (SEQ. ID. NO. 1) sequence motifs are, for example, the cytoskeleton-associated proteins zyxin and vinculin or the surface protein ActA of the facultative intracellular bacterium *Listeria monocytogene*. Owing to the interaction of the EVH1 domains of VASP and the FPPPP ~~motives~~ (SEQ. ID. NO. 1) motifs in the EVH1 binding domain of zyxin, there is an interaction between zyxin and VASP. --

Replace current paragraph 7 at page 3 with the following paragraph:

-- In cultivated cells, VASP is associated with cell-matrix contact sites (focal adhesion points), cell-cell contacts, and the actin filament system and dynamic membrane structures, for example, the midline of motile cells. A large amount of experimental data confirms that VASP provides profilactin, an adapter molecule, to sites with the cytoskeletal proteins zyxin and vinculin or with the surface protein ActA in cells infected with *Listeria spec.* The EVH1 domain binding FPPPP (SEQ. ID. NO. 1) motif in the proteins zyxin, vinculin and ActA and the EVH1 domain in VASP have been characterized functionally and structurally by NMR structure elucidation. --

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Replace current paragraph 8 at pages 3 and 4 with the following paragraph:

-- Functional studies confirm that VASP is a decisive factor for increased localized formation of actin filament. Thus, it is an important factor for the regulation of cell adhesion and cell motility, wherein VASP interacts directly with other proteins such as zyxin, vinculin or profilin. This was demonstrated, for example, by microinjection of peptides which contain the binding ~~motive~~ motif of the VASP-zyxin interaction. The VASP field is reviewed in Guidebook to the Cytoskeletal and Motor Proteins (Eds., Kreis,T., and Vale,R.), Oxford University Press, (1999) at pp. 168 –171. For these reasons, the complex between VASP and zyxin is considered to be a novel potential target structure which can be used for influencing disorders associated with pathological changes in cell adhesion and cell motility. For example, arteriosclerosis and coagulation disorders and the associated cardiovascular disorders may be treated with appropriate medicaments for modulating this interaction. Accordingly, VASP and zyxin or homologues or derivatives of these proteins which interact with one another can be used, *inter alia*, to identify chemical substances which can be used as therapeutically active compounds for treating cardiovascular disorders. --

Replace current paragraph 30 at page 13 with the following paragraph:

-- The invention further relates to a chemical compound for modulating the interaction between an EVH1 binding domain or a protein having an EVH1 binding domain and an EVH1 domain or a protein having an EVH1 domain which was identified by a process of the present invention, as described above. Such chemical compounds are preferably peptides, in particular with the sequences FPPPP (SEQ. ID. NO. 1) or WPPPP (SEQ. ID. NO. 2), or their chemical derivatives and proline-rich homologues. Such chemical

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~~compound~~ compounds can be medicaments for the treatment of the disorders described above. --

Replace current paragraph 53 at pages 21 and 22 with the following paragraph:

-- Thus far, there are no known non-peptidergic inhibitors of the VASP/zyxin interaction. To simulate the action of potential inhibitors, inhibition experiments were carried out using competing peptides which contained the VASP binding motif of zyxin (FPPPP (SEQ. ID. NO. 1)). In earlier works (Niebuhr et al. (1997) EMBO J. 16, 5433) mutations in this motif and their effect on the inhibition of the VASP/ActA interaction, which is also based on the binding of VASP to FPPPP (SEQ. ID. NO. 1) motifs in ActA, were studied. It was found that peptides having an APPPP (SEQ. ID. NO. 3) motif showed considerably worse inhibition when compared to the wild type sequence FPPPP (SEQ. ID. NO. 1), whereas peptides having a WPPPP motif had an even better inhibition that the wild type motif (inhibition: WPPPP (SEQ. ID. NO. 2) > FPPPP (SEQ. ID. NO. 1) > APPPP (SEQ. ID. NO. 3)). Zyxin peptides having corresponding mutations were used to compete with the VASP/zyxin interaction. For the apparent inhibition constants of the peptides, the same sequence was found as for the VASP/ActA interaction (Fig. 2): WPPPP (SEQ. ID. NO. 2) > FPPPP (SEQ. ID. NO. 1) > APPPP (SEQ. ID. NO. 3). --

Replace current paragraph 60 at page 25 with the following paragraph:

-- For the homogenous assay, human VASP having a complete amino acid sequence, isolated from insect cells (SF21), was used. The binding of specific antibodies to the VASP provided a fluorescent label. The binding partners used initially were peptides having the VASP binding ~~motive~~ motif FPPPP (SEQ. ID. NO. 1) which were likewise capable of binding to the other fluorophor for the energy transfer through coupled biotin

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(streptavidin-APC). However, in subsequent experiments, the VASP binding partner used was, instead of peptides, a GST fusion protein with the N-terminus of zyxin (GST-zyxin(1-142)) which contained several of these FPPPP (SEQ. ID. NO. 1) ~~motives~~ motifs. To this end, GST-zyxin(1-142) was expressed in *E. coli*, purified, and covalently modified with biotins. Thus, it was possible to measure a transfer of energy between the fluorescently labeled binding partners. --

Replace current paragraph 64 at page 25 with the following paragraph:

-- Fig. 2: Inhibition of the VASP/zyxin interaction by competing peptides containing the APPPP (SEQ. ID. NO. 3), FPPPP (SEQ. ID. NO. 1), or WPPPP (SEQ. ID. NO. 2) ~~motive~~ motif. --

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